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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/715,909	11/17/2000	Ronald D. Flannagan	35718/204664	5613

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EXAMINER
HAYES, ROBERT CLINTON

ART UNIT	PAPER NUMBER
1647	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/715,909	Applicant(s) Flannagan et al
	Examiner Robert C. Hayes, Ph.D.	Art Unit 1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 16, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-3, 7, 8, 10-18, and 26-36* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3, 7, 8, 10-18, and 32-36* is/are rejected.

7) ☒ Claim(s) *26-31* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. The amendment filed 1/06/03 has been entered.

2. The rejection of claims 15-16 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn due to the amendment of the claims.

3. The rejection of claims 1-3, 7-8, 10-18 & 26-36 under 35 U.S.C. 112, first paragraph, as containing new subject matter is withdrawn due to the amendment of the claims.

4. The rejection of claims 26-31 under 35 U.S.C. 112, first paragraph, for lack of written description is withdrawn due to the amendment of the claims.

5. The rejection of claims 1-3, 7-8 & 10-18 under 35 U.S.C. 112, second paragraph, as it relates to "hybridization" is withdrawn due to the amendment of the claims.

6. The rejection of claims 1-3, 7-8, 10-18, 26-29 & 33-35 under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of "at least about" is withdrawn due to the amendment of the claims.

7. Applicants' arguments filed 1/06/03 have been considered but are not found persuasive.

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. Claims 26-31 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

10. Claims 1-3, 7-8, 10-18 & 32-36 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed, for the reason made of record in Paper Nos: 10 (mailed 2/13/02) & 13 (mailed 10/18/02), and as follows.

Applicants argue on pages 7-11 of the response that "the Examiner has continued to require that the Applicants disclose each sequence falling within the claimed genus", and cites MPEP 707.07(f). In contrast to Applicants' arguments, this assertion is a mischaracterization of the record. The issue is that although those claims that recite either a given % identity or hybridization claim language, as it relates to a specific SEQ ID NO and appropriate functional language, do comply with the Written Description Guidelines referenced in the previous Office

action, claims 1g , 7g & 32, etc. do not structurally constitute an open reading frame, nor does the specification adequately describe a genus that merely constitutes "at least 22 contiguous nucleotides of... SEQ ID NO:1" or that encodes... "at least 25 contiguous [amino acid] residues", fused to undescribed heterologous nucleotide sequences, etc. "of interest", which alternatively encompass undescribed 5' or 3' flanking or enhancer regions, introns, allelic variants, or other sequences "comprising" any insect receptor-related nucleic acid sequence fragment; thereby, not meeting the written description requirements under 35 U.S.C. 112, first paragraph (i.e., for these generic heterologous nucleotide sequences that Applicants have chosen to recite in a Markush format). In contrast, the specification describes fragments that bind Bt toxin as consisting of at least the extracellular part of this receptor (e.g., see pages 19 and 35 of the specification), and that the "Cry1A binding site is encoded by residues 4038-4547 of SEQ ID NO:1 (i.e., at least 510/3= 170 specific amino acid residues), which the claims alternatively do not currently reflect.

As Applicants' correctly point out on pages 8-10 of the response, analogous to the situation decided in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself". Additionally, the court held in *Univ. California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) that:

"One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have

previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is".

and that:

"A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, *defined by nucleotide sequence*, falling in the scope of the genus or of a recitation of structural features common to the members of the genus, *which features constitute a substantial portion of the genus* [emphasis added]. This is analogous to enablement of a genus under 112, [first paragraph], by showing the enablement of a representative number of species within the genus. See Angstadt, 537 F.2d at 502-03, 190 USPQ at 218".

In contrast, an invitation for others to discover a representative number of species with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics has not reasonably been provided within the instant specification. In other words, claims directed toward heterologous nucleotide sequence merely comprising a few nucleotides of SEQ ID NO:1, or which merely claim "encoding a fusion polypeptide comprising *at least one polypeptide of interest*" when none are described, does reasonably support the contention that Applicants' are in possession of such broad claims comprising generic heterologous sequences with little structural characteristics, in contrast to that described within the specification as it relates to the complete open reading frame represented by SEQ ID NO:1.

Thus, Appellants were not reasonably in possession of the claimed genus of *Lepidopteran* receptor proteins, as it relates to claims reciting "at least 22 contiguous nucleotides of... SEQ ID NO:1" or that encodes... "at least 25 contiguous [amino acid] residues"(i.e., as it relates to claims 1g, 7g & 32); especially when "the effect will be evaluated by routine screening assays" is

alternatively a consideration under enablement, and not written description (i.e., as it relates to Applicants' comments on page 10-11 of the response).

Applicants are again directed toward the Revised Interim Utility and Written Description Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999 (i.e., see Examples 6 & 7).

11. Claims 1-3, 7-8, 10-18 & 32 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific polypeptide depicted as SEQ ID NO:2, does not reasonably provide enablement for any biological functional equivalent polypeptides/ fragments with little structural characterization and no distinguishable recited functional characteristics. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for the reason made of record in Paper Nos: 10 (mailed 2/13/02) & 13 (mailed 10/18/02), and as follows.

Applicants' argue on pages 11-13 of the response that "applicants have argued that the specification provides a rationale scheme for determining the regions of the *B*t toxin receptor that would tolerate modification", that "the standard for enablement set forth in the Office Action is not supported by the applicable case law" as it relates to "if experimentation... is undue", and cites *In re Angstadt* and *In re Wands.* However, Applicants' assertions that the Examiner has argued that "applicant [must] identify every functional fragment of the disclosed sequences so

that no experimentation is required to make and use these fragments" mischaracterizes the rejection made of record. In contrast to Applicants' assertions, the guidance provided by the specification is that a fragment that does not consist of at least the extracellular part of this receptor would not reasonably bind Bt toxin (e.g., see pages 19 and 35 of the specification), and that the "Cry1A binding site is encoded by residues 4038-4547 of SEQ ID NO:1 (i.e., at least 510/3= 170 specific amino acid residues). Therefore, consistent with the court's holding *in In re Wands,* which requires guidance more than a mere invitation for others to "make and test", the claims are not reasonably commensurate in scope with that disclosed in the specification because 22 nucleotides merely encode 7 random amino acid residues, which is not the 170 specific encoded amino acid residues the specification itself states must be encoded to result in a functional invention. Moreover, as previously made of record, neither 22 nucleotides (i.e., as it relates to claims 1g & 32) nor 25 encoded amino acid residues (i.e., as it relates to claim 7g) would reasonably constitute the extracellular domain for this claimed encoded receptor, based on what's known within the art at the time of filing Applicants' invention. Nor would such reasonably constitute an encoded polypeptide of "approximately 210 and 205 kDa", as it relates to the specific guidance provided on page 34 of the specification concerning the critical amino acids required to "bind Cry1A(b)". In contrast, the current claims still encompass random "substitutions, deletions, truncations, and insertions" to the encoded polypeptide of SEQ ID NO:2 (e.g., see pages 15-17 of the specification), and such random mutations to the nucleotide sequence of SEQ ID NO:1 would alternatively reasonably result in an inactive encoded protein;

consistent with the teachings of Skolnick, Fetrow and Rudinger previously made of record. Therefore, because the claims are not commensurate in scope with minimally requiring nucleotide residue numbers 4038-4547 of SEQ ID NO:1, and alternatively recite insufficient structural characteristics to reasonably enable the invention for encoding the critical CrylA(b) binding domain, it would reasonably require undue experimentation for the skilled artisan to known how to make and use the invention as currently and broadly claimed, for the reasons made of record.

Lastly, in contrast to Applicants' contentions on page 13 of the response that references (i.e., Rudinger) are not representative of the state of the art at the time of the instant invention merely due to their age is not relevant, no documentary evidence to the contrary has been made of record, nor has any evidence been provided that teaches away from that taught by Rudinger. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977). Nevertheless, the teachings of Skolnick et al. (2000) have already been made of record, in which:

"Sequence-based methods for functional prediction are inadequate because of the multifunctional nature of proteins. Proteins can gain and lose function during evolution and may, indeed, have multiple functions in the cell (Box 1). Sequence-to-function methods cannot specifically identify these complexities. Inaccurate use of sequence-to-function methods has led to significant function-annotation errors in the sequence databases". (e.g., see page 34).

Thus, Applicants' arguments are not persuasive, for the reasons made of record.

12. Claims 7-8 (and those claims dependent on claim 7) stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the

subject matter which applicant regards as the invention, because it remains ambiguous what metes and bounds constitute "at least one polypeptide *of interest*", in which use of this relative terms further defines nothing, and therefore, remains indefinite.

It is noted that Applicants did not address this particular rejection.

13. Claims 1-3, 7-8 & 10-16 stand rejected under 35 U.S.C. 102(b) as being anticipated by Bulla et al. (U.S. Patent 5,693,491), for the reasons made of record in Paper No: 13 (mailed 10/18/02), and as follows.

Applicants argue on pages 14-15 of the response that "[t]he nucleotide sequence encoding the receptor [of Bulla et al] shares short regions of identity with SEQ ID NO:1". The Examiner agrees. Applicants then argue various amendments to the claims, which the Examiner agrees obviates the rejection to some members of the Markush group recited in claim 1 . However, because by definition, "short regions of identity with SEQ ID NO:1" hybridize under stringent conditions to Bulla's DNA with the functional ability to bind CryA1(b), in which A hybridizes to T residues and G hybridizes to C residues (e.g., see page 29 of the specification), the limitations of the claims related to hybridization under stringent conditions remains anticipated by Bulla.

In summary, Bulla et al. teach a receptor for a Bt toxin (Cry1A(b); as it relates to claims 2-3) from *M. sexta* that is 63.9 % identical to SEQ ID NO:1 (col. 2) and encodes a polypeptide that is 60.7 % identical to SEQ ID NO:2. In that nucleotide residue #s 978-993, 1524-1544, 1555-1572, 2511-2530, etc. are 100% identical, the limitation of "hybridizes under stringent

conditions to SEQ ID NO:1", etc. is inherently met (i.e., as it relates to claim 1(h)), where such a nucleotide sequence "encodes a fusion protein" of a "toxin receptor" (i.e., as it relates to claim 8) for Bulla's polynucleotide sequences fused to these hybridizing residues (i.e., as it relates to claim 7h). In that Bulla et al. disclose expression cassettes/ vectors and transformed cells comprising this nucleic acid molecule, which include insect and mammalian cells, as well as microorganisms/procaryotic cells/*E. coli*, claims 7-8 & 10-16 are further anticipated (i.e., cols. 4-5).

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
March 27, 2003

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